

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-32 (Canceled).

33. (Previously presented) A method of inducing cellular expansion, comprising the steps of:

- isolating a population of cells to be expanded; and
- exposing said cells to a soluble mutant flt3-L polypeptide to produce an expanded cell population, wherein said polypeptide comprises a substitution at one or more residues corresponding to amino acid position 24 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) or amino acid positions 8-15, 81-87 or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18), wherein the mutant flt3-L polypeptide exhibits increased biological activity relative to full length wild type (SEQ ID NO:1) or mature human wild type (SEQ ID NO:18) flt3-L polypeptide.

34. (Previously presented) The method of claim 33, wherein the expanded cell population is introduced into a patient.

35. (Original) The method of claim 33, wherein the population of cells to be expanded comprises hematopoietic cells.

36. (Original) The method of claim 33, wherein the population of cells is also exposed to a growth factor in addition to said flt3-L mutant polypeptide.

37. (Original) The method of claim 33, wherein said growth factor is selected from the group consisting of interleukins, colony stimulating factors, and protein kinases.

38. (Previously presented) A method of expanding a population of cells *in vivo*, comprising the step of administering to a subject a pharmaceutical composition of a soluble mutant flt3-L polypeptide sufficient to induce the expansion of a target cell population, wherein said polypeptide comprises a substitution at one or more residues corresponding to amino acid position 24 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) or amino acid positions 8-15, 81-87 or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18), wherein the mutant flt3-L polypeptide exhibits increased biological activity relative to full length wild type (SEQ ID NO:1) or mature human wild type (SEQ ID NO:18) flt3-L polypeptide.

39. (Currently amended) The method of claim 38, wherein the target cell population ~~is isolated from the group consisting of~~ comprises hematopoietic cells, ~~NK-cells~~ or dendritic cells.

40. (Original) The method of claim 38, wherein the pharmaceutical composition further comprises a growth factor in addition to said flt3-L mutant polypeptides.

41. (Original) The method of claim 40, wherein said growth factor is selected from the group consisting of interleukins, colony stimulating factors and protein kinases.

Claims 42-68 (Canceled)

69. (Previously presented) The method according to claim 33, wherein a basic amino acid within amino acid positions 8-15 or 81-87 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with a non-basic amino acid or wherein an amino acid within amino acid positions 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with a basic amino acid.

70. (Previously presented) The method according to claim 69, wherein the basic amino acid replaced within amino acid positions 8-15 or 81-87 is the His at position 8 or the Lys at position 84 of the mature human wild type flt3-L (SEQ ID NO:18).

71. (Previously presented) The method according to claim 33, wherein a second polypeptide is fused to the soluble mutant flt3-L polypeptide, wherein said second polypeptide is erythropoietin (EPO), thrombopoietin (TPO), granulocyte-macrophage Colony Stimulating Factor (GM-CSF), granulocyte Colony Stimulating Factor (G-CSF), an interleukin, an immunoglobulin, or fragments thereof, wherein the fragments retain the biological activity of the second polypeptide.

72. (Previously presented) The method according to claim 33, wherein said substitution at one or more residues corresponds to amino acid positions 8, 84, 118 or 122 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).

73. (Previously presented) The method according to claim 33, wherein said soluble mutant flt3-L polypeptide comprises one or more substitutions corresponding to L1H (SEQ ID NO:10), H8Y (SEQ ID NO:11), W118R (SEQ ID NO:16), K84E (SEQ ID NO:14), K84T (SEQ ID NO:15) or Q122R (SEQ ID NO:17).

74. (Previously presented) The method according to claim 33, wherein said soluble mutant flt3-L polypeptide comprises amino acids 28-160, 28-182 or 28-185 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1).

75. (Previously presented) The method according to claim 38, wherein a basic amino acid within amino acid positions 8-15 or 81-87 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with a non-basic amino acid or wherein an amino acid within amino acid positions 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with a basic amino acid.

76. (Previously presented) The method according to claim 75, wherein the basic amino acid replaced within amino acid positions 8-15 or 81-87 is the His at

position 8 or the Lys at position 84 of the mature human wild type flt3-L (SEQ ID NO:18).

77. (Previously presented) The method according to claim 38, wherein a second polypeptide is fused to the soluble mutant flt3-L polypeptide, wherein said second polypeptide is erythropoietin (EPO), thrombopoietin (TPO), granulocyte-macrophage Colony Stimulating Factor (GM-CSF), granulocyte Colony Stimulating Factor (G-CSF), an interleukin, an immunoglobulin, or fragments thereof, wherein the fragments retain the biological activity of the second polypeptide.

78. (Previously presented) The method according to claim 38, wherein said substitution at one or more residues corresponds to amino acid positions 8, 84, 118 or 122 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).

79. (Previously presented) The method according to claim 38, wherein said soluble mutant flt3-L polypeptide comprises one or more substitutions corresponding to L1H (SEQ ID NO:10), H8Y (SEQ ID NO:11), W118R (SEQ ID NO:16), K84E (SEQ ID NO:14), K84T (SEQ ID NO:15) or Q122R (SEQ ID NO:17).

80. (Previously presented) The method according to claim 38, wherein said soluble mutant flt3-L polypeptide comprises amino acids 28-160, 28-182 or 28-185 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1).

Claims 81-110 (Canceled)

111. (Currently amended) A method for transplanting hematopoietic stem cells, progenitor cells or both hematopoietic stem cells and progenitor cells in a patient in need thereof, comprising:

(a) administering a therapeutically effective amount of a pharmaceutical composition ~~[[of]]~~comprising a soluble flt3-L mutant polypeptide to the patient to expand the hematopoietic stem cells, progenitor cells or both in the patient, wherein said polypeptide has a substitution at one or more residues corresponding to amino acid position 24 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) or amino acid positions 8-15, 81-87 or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) wherein the mutant flt3-L polypeptide exhibits increased biological activity relative to full length wild type (SEQ ID NO:1) or mature human wild type (SEQ ID NO:18) flt3-L polypeptide; ~~and~~

(b) collecting said expanded hematopoietic stem cells, progenitor cells or both from the patient; and

(c) transplanting hematopoietic stem cells, progenitor ~~said~~ cells collected in step (b) or both to the patient.

112. (Currently amended) The method according to claim 111, further comprising administering radiation, chemotherapy or both radiation and chemotherapy

to the patient, wherein said cells are transplanted concurrent with or following administering radiation, chemotherapy or both.

113. (Previously presented) The method according to claim 111, wherein the hematopoietic stem cells or progenitor cells are allogeneic.

114. (Previously presented) The method according to claim 111, wherein the hematopoietic stem cells or progenitor cells are autologous.

115. (Previously presented) The method according to claim 111, wherein a basic amino acid within amino acid positions 8-15 or 81-87 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with a non-basic amino acid, or wherein an amino acid within amino acid positions 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with a basic amino acid.

116. (Previously presented) The method according to claim 115, wherein the basic amino acid replaced within amino acid positions 8-15 or 81-87 is the His at position 8 or the Lys at position 84 of the mature human wild type flt3-L (SEQ ID NO:18).

117. (Previously presented) The method according to claim 115, wherein the amino acid replaced within amino acid positions 116-124 is the Trp at position 118 or the Gln at position 122 of the mature human wild type flt3-L (SEQ ID NO:18).

118. (Previously presented) The method according to claim 111, wherein a second polypeptide is fused to the soluble mutant flt3-L polypeptide, wherein said second polypeptide is erythropoietin (EPO), thrombopoietin (TPO), granulocyte-macrophage Colony Stimulating Factor (GM-CSF), granulocyte Colony Stimulating Factor (G-CSF), an interleukin, an immunoglobulin, or fragments thereof, wherein the fragments retain the biological activity of the second polypeptide.

119. (Previously presented) The method according to claim 111, wherein said substitution at one or more residues corresponds to amino acid positions 8, 84, 118 or 122 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).

120. (Previously presented) The method according to claim 111, wherein said soluble mutant flt3-L polypeptide has one or more substitutions corresponding to L1H (SEQ ID NO:10), H8Y (SEQ ID NO:11), W118R (SEQ ID NO:16), K84E (SEQ ID NO:14), K84T (SEQ ID NO:15) or Q122R (SEQ ID NO:17).

121. (Previously presented) The method according to claim 111, wherein said soluble mutant flt3-L polypeptide comprises amino acids 28-160, 28-182 or 28-185 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1).

122. (Currently amended) A method for transplanting hematopoietic stem cells, progenitor cells or both hematopoietic stem cells and progenitor cells in a patient in need thereof, comprising:

- (a) collecting hematopoietic cells, progenitor cells or both from the patient;
- (b) administering ex vivo a therapeutically an effective amount of a pharmaceutical composition ~~[[of]]~~comprising a soluble flt3-L mutant polypeptide to said cells collected in step (a) to expand the ~~[[to]]~~hematopoietic stem cells, progenitor cells or both hematopoietic stem cells and progenitor cells, wherein said polypeptide has a substitution at one or more residues corresponding to amino acid position 24 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) or amino acid positions 8-15, 81-87 or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) wherein the mutant flt3-L polypeptide exhibits increased biological activity relative to full length wild type (SEQ ID NO:1) or mature human wild type (SEQ ID NO:18) flt3-L polypeptide; and
- ~~(((b))~~c) transplanting said expanded hematopoietic stem cells, progenitor cells or both to the patient.

123. (Currently amended) The method according to claim 122, further comprising administering radiation, chemotherapy or both radiation and chemotherapy to the patient, wherein said cells are transplanted concurrent with or following administering radiation, chemotherapy or both.

124. (Previously presented) The method according to claim 122, wherein the hematopoietic stem cells or progenitor cells are allogeneic.

125. (Previously presented) The method according to claim 122, wherein the hematopoietic stem cells or progenitor cells are autologous.

126. (Previously presented) The method according to claim 122, wherein a basic amino acid within amino acid positions 8-15 or 81-87 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with a non-basic amino acid, or wherein an amino acid within amino acid positions 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with a basic amino acid.

127. (Previously presented) The method according to claim 126, wherein the basic amino acid replaced within amino acid positions 8-15 or 81-87 is the His at position 8 or the Lys at position 84 of the mature human wild type flt3-L (SEQ ID NO:18).

128. (Previously presented) The method according to claim 126, wherein the amino acid replaced within amino acid positions 116-124 is the Trp at position 118 or the Gln at position 122 of the mature human wild type flt3-L (SEQ ID NO:18).

129. (Previously presented) The method according to claim 122, wherein a second polypeptide is fused to the soluble mutant flt3-L polypeptide, wherein said

second polypeptide is erythropoietin (EPO), thrombopoietin (TPO), granulocyte-macrophage Colony Stimulating Factor (GM-CSF), granulocyte Colony Stimulating Factor (G-CSF), an interleukin, an immunoglobulin, or fragments thereof, wherein the fragments retain the biological activity of the second polypeptide.

130. (Previously presented) The method according to claim 122, wherein said substitution at one or more residues corresponds to amino acid positions 8, 84, 118 or 122 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).

131. (Previously presented) The method according to claim 122, wherein said soluble mutant flt3-L polypeptide has one or more substitutions corresponding to L1H (SEQ ID NO:10), H8Y (SEQ ID NO:11), W118R (SEQ ID NO:16), K84E (SEQ ID NO:14), K84T (SEQ ID NO:15) or Q122R (SEQ ID NO:17).

132. (Previously presented) The method according to claim 122, wherein said soluble mutant flt3-L polypeptide comprises amino acids 28-160, 28-182 or 28-185 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1).

Claim 133 (Canceled)

134. (Previously presented) The method according to claim 69, wherein the amino acid replaced within amino acid positions 116-124 is the Trp at position 118 or the Gln at position 122 of the mature human wild type flt3-L (SEQ ID NO:18).

135. (Previously presented) The method according to claim 75, wherein the amino acid replaced within amino acid positions 116-124 is the Trp at position 118 or the Gln at position 122 of the mature human wild type flt3-L (SEQ ID NO:18).

Claims 136-141 (Canceled)

142. (New) The method according to claim 33, wherein the population of cells to be expanded comprise CD34⁺ hematopoietic stem cells, hematopoietic progenitor cells, hematopoietic stem and progenitor cells or dendritic cells.

143. (New) The method of claim 111, further comprising administering said composition to the patient after transplanting said cells to the patient.

144. (New) The method according to claim 122, further comprising administering said composition to the patient prior to collecting the hematopoietic cells from the patient.

145. (New) The method according to claim 122, further comprising administering said composition to the patient after transplanting the hematopoietic stem cells, progenitor cells or both to the patient.

146. (New) The method according to claim 122, wherein the hematopoietic cells are collected from peripheral blood, umbilical cord blood or bone marrow.

147. (New) The method according to claim 122, wherein the hematopoietic stem cells, progenitor cells or both are CD34⁺.

148. (New) The method according to claim 39, wherein the hematopoietic cells comprise hematopoietic stem cells, hematopoietic progenitor cells, or hematopoietic stem and progenitor cells.

149. (New) The method according to claim 148, wherein the hematopoietic cells are CD34⁺.

150. (New) The method of claim 142, wherein the expanded cell population is introduced into a patient.